REMARKS

Status of the Claims

Claims 1-8, 10, 12 and 14-36 are currently pending in the application. Claims 1-7, 9-13 and 28-33 stand rejected. The Examiner objects to several claims. Claims 8 and 14-27 are withdrawn as being drawn to a non-elected invention. Claims 1-8, 10, 12, 28-31 and 33 have been amended as set forth herein. Claims 9, 11 and 13 have been cancelled herein. All amendments and cancellations are made without prejudice or disclaimer. New claims 34-36 have been added herein. No new matter has been added by way of the present amendments.

Specifically, the amendment to claims 1, 28, 29 and 30 are supported by original claims 8 and 11 as well as the specification at, for instance, page 14, lines 19-22.

New claim 34 is supported by the specification at least at page 20, lines 22-24.

New claim 35 is supported by the specification at least at page 19, lines 8-12.

New claim 36 is supported by the specification at least at page 35, lines 16-18.

Reconsideration is respectfully requested.

Objections to the Claims

The Examiner objects to the claims because they "contain multiple grammatical errors." (*See*, Office Action of May 11, 2007, at page 2, hereinafter, "Office Action"). Applicants thank the Examiner for careful review and consideration of the pending claims and have attempted to address the "grammatical errors" by way of the present amendment.

Applicants believe the presently amended claims address all of the grammatical errors. All amendments to the claims do not add new matter to the claims and are fully supported by the specification as indicated, above.

Therefore, reconsideration and withdrawal of the objection to the claims are respectfully requested.

Information Disclosure Statement

The Examiner states that the reference "CD" of the Information Disclosure Statement (IDS) of May 12, 2006 was not considered because no reference was provided. Pursuant thereto, Applicants attach hereto a copy of the reference for the Examiner's convenience. Consideration thereof is respectfully requested. The copy provided corresponds to the English language version of the Russian publication.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-7, 9-13 and 28-33 stand rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (*See*, Office Action, at pages 2-4). Claims 9, 11 and 13 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims as set forth herein.

The Examiner provides items A) through I) which require correction. In general, although Applicants do not agree that the claims are indefinite, to expedite prosecution, the claims have been amended herein without prejudice or disclaimer to address all of the

Examiner's items. Regarding item C), Applicants note that claim 1 has been amended herein to recite a specific active step. Further amendment of this claim is supported by original claims 8 and 11, as well as the specification at page 14, lines 19-22.

Furthermore, it is believed that new claims 34-36 are consistent with these corrections.

In light of the claim amendments, reconsideration and withdrawal of the indefiniteness rejection of claims 1-8, 10, 12 and 28-33 are respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Written Description

Claims 1-7, 9, 10, 12, 13 and 28-33 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the written description requirement. (*See*, Office Action, at pages 4-5). Claims 9 and 13 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims as set forth herein.

The Examiner states that Applicants have not provided sufficient written description support to show Applicants had possession of (knowledge of) all possible fragments of fibronectin encompassed by the scope of the presently claimed invention, especially fragments of fibronectin having an unlimited number of substitutions, deletions, insertions or additions.

Although Applicants do not believe the claims lack written description support in the specification, to expedite prosecution, claims 1 and 28-30 have been amended herein without prejudice or disclaimer to recite fibronectin fragments having specific sequences, SEQ ID NOS:

1-19 and variants wherein one or more amino acids are substituted according to the substitutions recited on page 14, lines 19-22 of the specification.

Since no specific reasoning is provided for the rejection of dependent claims 2-7, 10, 12, 31 or 32, these dependent claims are believed to also comply with the written description requirements as, *inter alia*, depending from a fully described base claim, amended claims 1 and 28-30.

Reconsideration and withdrawal of the written description rejection of claims 1-7, 10, 12 and 28-33 are respectfully requested.

Enablement

Claims 1-7, 9, 10, 12, 13 and 28-33 stand rejected under 35 U.S.C. § 112, first paragraph, for failing to comply with the enablement requirement. (*See*, Office Action, at pages 5-7). Claims 9 and 13 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims as set forth herein.

The Examiner states that the specification fully enables one of ordinary skill in the art to practice the invention directed to a method for preparing cytotoxic lymphocytes in the presence of fibronectin or a fibronectin fragment comprising SEQ ID NO:12. The remainder of the Examiner's comments concerning the grounds of the enablement rejection appear to be similar to the comments made concerning the written description rejection. That is, the Examiner believes the specification does not fully enable all possible fragments of fibronectin encompassed by the present claims.

Although Applicants do not believe the claims lack enablement support in the specification, to expedite prosecution, claims 1 and 28-30 have been amended herein without prejudice or disclaimer to recite fibronectin fragments having specific sequences, SEQ ID NOS: 1-19 and variants wherein one or more amino acids are substituted according to the substitutions recited on page 14, lines 19-22 of the specification.

Since no specific reasoning is provided for the rejection of dependent claims 2-7, 10, 12, 31 or 32, these dependent claims are believed to also enabled as, *inter alia*, depending from a fully enabled base claim, amended claims 1 and 28-30.

Reconsideration and withdrawal of the enablement rejection of claims 1-7, 10, 12 and 28-33 are respectfully requested.

Rejections Under 35 U.S.C. § 102(b)

Claims 1-6, 9-13 and 28-33 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Pollok et al., *J. Virol.* 72:4882-4892, 1998 (hereinafter, "Pollok et al."). (*See*, Office Action, at page 8). Claims 9, 11 and 13 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims as set forth herein.

The Examiner states that Pollock et al. disclose at page 4883 incubating T lymphocytes in the presence of a fibronectin fragment called CH-296. Because the T lymphocytes disclosed in Pollok et al. are $CD8^+$, the Examiner concludes these cells are cytotoxic lymphocytes. (See page 4884 of Pollok et al.).

Although Applicants do not believe the claims are anticipated by the cited reference, to expedite prosecution, the terms "inducing" and "maintaining" have been removed from the claims without prejudice or disclaimer. Instead, the claims are now directed to a step of "expanding." Pollok et al. do not disclose expanding lymphocytes in the presence of a fibronectin fragment as defined by amended independent claims 1 and 28-30.

Dependent claims 2-6, 10, 12 and 31-33 are believed to not be anticipated as, *inter alia*, depending from a non-anticipated base claim, amended claims 1 and 28-30.

Reconsideration and withdrawal of the anticipation rejection of claims 1-6, 10, 12 and 28-33 are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-7, 9-13, 28-30 and 33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable as obvious over Ostergaard et al., *European J. Immunol.*, 25:252-256, 1995 (hereinafter, "Ostergaard et al.") in view of Taguchi et al., U.S. Patent No. 5,198,423 (hereinafter, "Taguchi et al.") as evidenced by Nunclon product information, VWRLabshop, page 1. (*See*, Office Action, at pages 8-10). Claims 9, 11 and 13 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection of these claims. Applicants traverse the rejection as to the remaining claims as set forth herein.

The Examiner states that Ostergaard et al. do not disclose or suggest a fibronectin fragment comprising SEQ ID NO:12 or immobilizing fibronectin on a Petri dish, flask or bag. However, the Examiner states that Taguchi et al. disclose or suggest a fibronectin fragment comprising SEQ ID NO:12 (at columns 3 and 4) and its advantages over full length fibronectin.

Additionally, the Examiner states that when these two disclosures are combined with the knowledge of one of ordinary skill in the art concerning Petri dishes, cell culture flasks and bags, one of ordinary skill in the art would have found the presently claimed invention to be obvious.

Although Applicants do not believe the claims are obvious in light of the cited references, to expedite prosecution, the terms "inducing" and "maintaining" have been removed from the claims without prejudice or disclaimer. Instead, the claims are now directed to a step of "expanding." The cited references do not disclose or suggest expanding lymphocytes in the presence of a fibronectin fragment as defined by amended independent claims 1 and 28-30, which includes a fibronectin fragment having a sequence of SEQ ID NO:12.

Furthermore, Ostergaard et al. actually discloses that CTL are degranulated by culturing cytotoxic cells in the presence of anti-CD3 antibody and fibronectin. In this reference, however, only 4 hours of culturing at the longest is carried out using $CD8^+$ T cell clones under such conditions so that expansion of cytotoxic lymphocyte as in the present invention is never carried out therein.

In contrast, the presently claimed invention is characterized in the step of expanding cytotoxic lymphocytes in the presence of a fibronectin fragment. Thereby, the expansion ratio is improved, expression of IL-2 receptor is enhanced, and the ratio of $CD8^+$ T cells is improved. In the step of culturing disclosed in Ostergaard et al., it is unknown whether or not expression of IL-2 receptor has been enhanced. Furthermore, Ostergaard et al. utilize CTL clones ($CD8^+$ cells) so that all the obtained cells are $CD8^+$ cells. Accordingly, an improvement in the ratio of $CD8^+$ T cells as in the present invention cannot be confirmed. Also, it is difficult in only 4 hours of culturing, as disclosed in Ostergaard et al., to obtain lymphocytes as many as obtained in the

present invention so that the effect of improving the expansion ratio in the present invention is not obvious over Ostergaard et al.

Therefore, reconsideration and withdrawal of the obviousness rejection of claims 1-7, 10, 12, 28-30 and 33 are respectfully requested.

Rejections Under the Obviousness-Type Double Patenting Doctrine

Claims 1-7, 9-13 and 28-33 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 7, 8, 14, 15, 24, 25 and 28 of copending U.S. Patent Application Serial No. 10/486,512, in view of U.S. Patent No. 5,198,423 and Chen et al., and claims 1-15, 20 and 21 of U.S. Patent Application Serial No. 10/568,745. (*See*, Office Action, at pages 10-12). Claims 9, 11 and 13 have been cancelled herein without prejudice or disclaimer, thus obviating the rejection of these claims. As to the remaining claims, the Examiner is respectfully requested to follow the procedure that is described in M.P.E.P. § 804(I)(B)(1), and reads as follows:

> If a "provisional" nonstatutory obviousness-type double patenting (ODP) rejection is the only rejection remaining in the earlier filed of the two pending applications, while the later-filed application is rejectable on other grounds, the examiner should withdraw that rejection and permit the earlier-filed application to issue as a patent without a terminal disclaimer. If the ODP rejection is the only rejection remaining in the later-filed application, while the earlier-filed application is rejectable on other grounds, a terminal disclaimer must be required in the later-filed application before the rejection can be withdrawn.
>
> If "provisional" ODP rejections in two applications are the only rejections remaining in those applications, the examiner should withdraw the ODP rejection in the earlier filed application thereby permitting that application to issue without need of a terminal disclaimer. A terminal disclaimer must be required in the later-filed application before the ODP rejection can be withdrawn and the application permitted to issue. If both applications are filed on the same day, the examiner

should determine which application claims the base invention and which application claims the improvement (added limitations). The ODP rejection in the base application can be withdrawn without a terminal disclaimer, while the ODP rejection in the improvement application cannot be withdrawn without a terminal disclaimer.

Accordingly, the Examiner is respectfully requested to issue a Notice of Allowance in this case and to address any possible double patenting issues in the co-pending applications.

CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Dated: October 11, 2007

Respectfully submitted,

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Attachments: PTO SB08 form
Copy of reference CD – "Animal cell culture: a practical approach" in an original form and a corresponding English version